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Bartonella species in small mammals and their potential vectors in Asia

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PEER REVIEW

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Comments

This is a good research about the presence of various species of *Bartonella* and its role at causing different infections. The consideration of authors to various reservoirs of this bacteria in animals that a little have been already surveyed is interesting. Diagnostic tests referred in this article are very useful.
Details on Page 764

ABSTRACT

In this article, authors review the current knowledge of *Bartonella* infection in small mammals including rodents, insectivores, bats and exotic small mammal pets and their vectors in Asia. Species of *Bartonella* are Gram-negative intracellular bacteria that infect erythrocytes of various mammalian and non-mammalian animals and mainly transmitted by blood sucking arthropod vectors. The genus *Bartonella* includes several species of important human diseases with severe clinical signs. Several new *Bartonella* species were isolated from rodents and other small mammals, and from human patients in Asia. *Bartonella* species are identified using standard polymerase chain reaction amplification and a sequencing targeting two housekeeping genes (gltA and rpoB) and the internal transcribed spacer fragment. Authors also discuss the implications in term of potential emerging zoonotic diseases.

KEYWORDS

Bartonella, Small mammals, Rodents, Shrews, Asia

1. Introduction

Member of the genus *Bartonella* are fastidious, hemotropic, Gram-negative and aerobic bacilli bacteria belonging to the class Alphaproteobacteria. Several species have been implicated in causing human diseases, ranging with short-term fever to severe endocarditis. Five species are known to be causative of significant human diseases: *Bartonella bacilliformis* (*B. bacilliformis*) is the causative agent of Oroya fever and verruga peruana (Peruvian wart); *Bartonella quintana* (*B. quintana*) is the causative agent of trench fever; *Bartonella henselae* (*B. henselae*) is the causative agent of cat-scratch disease[1-3]. Additionally, several species have been described as coincident zoonotic infection agents including *Bartonella alsatica* (*B. alsatica*) [4], *Bartonella koehlerae* (*B. koehlerae*)[5], *Bartonella vinsonii*

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subsp. *berkhoffii* (*B. vinsonii* subsp. *berkhoffii*)[6,7], *Bartonella tamiae* (*B. tamiae*)[8], *Bartonella rochalimae* (*B. rochalimae*)[9], *Bartonella washoensis* (*B. washoensis*)[10] and *Candidatus Bartonella mayotimonensis*[11].

Bartonella species parasitize the erythrocytes, endothelial cells, monocytes and dendritic cells of mammals[12,13]. Additionally, a *Bartonella* species has been described in loggerhead sea turtle[14]. Bacteria of the genus *Bartonella* are widespread in domestic and wild animals and are transmitted by a great variety of bloodsucking arthropods including fleas, mites, sand flies and ticks[15,16]. Since 1990s, numerous studies have demonstrated that several mammals such as cats, dogs, rabbits and rodents are potential reservoir hosts of *Bartonella*. Until now, new host species such as insectivores, bats and exotic pets are continually added in the reservoir hosts' list. This review provides an update of reservoir host species focusing on small mammals, their potential vectors and case reports of *Bartonella* infection in Asia, a hotspot of emerging infectious diseases[17,18]. Hosts such as cats, dogs, and rabbits have been excluded from this review since several review articles have been already written on these reservoir hosts[19,20].

2. Taxonomy and bacteriology of *Bartonella*

Bacteria of the genus *Bartonella* belong to the family Bartonellaceae, order Rhizobiales, class Alphaproteobacteria, and phylum Proteobacteria. *Bartonella* are closely related with *Brucella* species and *Agrobacterium tumefaciens*. *Bartonella* genus includes a large diversity of *Bartonella* species, which were identified from different host species. Since the development of more efficient molecular tools for detection, genetic criteria and species identification are greatly improved[21], and the description of new *Bartonella* species has rapidly increased over the last 10 years and is still continually growing. The genus currently contains more than 30 species and 3 subspecies including *B. alsatica*, *Bartonella australis*, *B. bacilliformis*, *Bartonella birtlesii* (*B. birtlesii*), *Bartonella bovis* (*B. bovis*), *Bartonella capreoli* (*B. capreoli*), *Bartonella chomelii*, *Bartonella coopersplainsensis* (*B. coopersplainsensis*), *Bartonella clarridgeiae* (*B. clarridgeiae*), *Bartonella doshiae* (*B. doshiae*), *Bartonella durdenii*, *Bartonella grahamii* (*B. grahamii*), *B. henselae*, *Bartonella japonica* (*B. japonica*), *B. koehlerae*, *Bartonella melophagi*, *Bartonella phoceensis* (*B. phoceensis*), *Bartonella queenslandensis* (*B. queenslandensis*), *Bartonella quintana* (*B. quintana*), *Bartonella rattaustraliani* (*B. rattaustraliani*), *Bartonella rattimassiliensis* (*B. rattimassiliensis*), *B. rochalimae*, *Bartonella schoenbuchensis*, *Bartonella silvatica* (*B. silvatica*), *Bartonella silvicola*, *B. tamiae*, *Bartonella taylorii* (*B. taylorii*), *Bartonella tribocorum* (*B. tribocorum*), *Bartonella vinsonii* subsp. *arupensis* (*B. vinsonii* subsp. *arupensis*), *B. vinsonii* subsp. *berkhoffii*, *Bartonella vinsonii* subsp. *vinsonii* (*B. vinsonii* subsp. *vinsonii*), *B. washoensis*, *Candidatus Bartonella antechini*, *Candidatus Bartonella mayotimonensis*, *Candidatus Bartonella thailandensis* (Table 1). Of these, several species may cause either asymptomatic or mild diseases or severe diseases. Bacteria from this genus are fastidious to grow *in vitro*. The culture on blood agar requires 7 to 45 d in primary isolation. Microscopically, the *Bartonella* species are Gram-negative bacilli. Several *Bartonella* species are flagellate, *B. bacilliformis*, *B. bovis* and *B. clarridgeiae*[22,23].

Table 1

List of the currently known described species of *Bartonella*.

Bartonella species	First detection	Country	Reference
B. alsatica	Wild rabbit	France	[59]
B. australis	Gray kangaroo	Australia	[60]
B. bacilliformis	Human	Europe	[61]
B. birtlesii	Mouse	German	[62]
B. bovis	Cow	France	[62]
B. capreoli	Deer	France	[63]
B. chomelii	Domestic cattle	France	[64]
B. clarridgeiae	Cat	USA	[65]
B. coopersplainsensis	Rat	Australia	[66]
B. doshiae	Field vole	United Kingdom	[67]
B. durdenii	Squirrel	USA	unpublished data
B. elizabethae	Human	USA	[68]
B. grahamii	Bank vole	United Kingdom	[67]
B. henselae	Cat	USA	[69]
B. japonica	Mouse	Japan	[70]
B. koehlerae	Cat	USA	[71]
B. melophagi	Sheep		unpublished data
B merieuxii	Canid	Irak	[72]
B. peromysci	Mouse		[67]
B. phoceensis	Wild rat	France	[73]
B. queenslandensis	Rat	Australia	[66]
B. quintana	Human		[74]
B. rattaustraliani	Rat	Australia	[66]
B. rattimassiliensis	Rat	France	[73]
B. rochalimae	Human	USA	[9]
B. schoenbuchensis	Deer	German	[75]
B. silvatica	Mouse	Japan	[70]
B. silvicola	Bat		unpublished data
B. talpae	Mole		[59]
B. tamiae	Human	Thailand	[6]
B. taylorii	Mouse	United Kingdom	[67]
B. tribocorum	Rat	France	[76]
B. vinsonii subsp. *arupensis*	Cattle		[77,78]
B. vinsonii subsp. *berkhoffii*	Dog		[79]
B. vinsonii subsp. *vinsonii*	Vole		[80]
B. volans	Squirrel	USA	unpublished data
B. washoensis	Human	USA	unpublished data

3. *Bartonella* genomes

The genome sizes of *Bartonella* species range from 1.5 to 2.5 Mb. Several *Bartonella* species including *B. bacilliformis*, *B. birtlesii*, *B. clarridgeae*, *B. grahamii*, *B. henselae*, *B. quintana*, *B. rattimassiliensis*, *B. rattaustraliani* and *B. tribocorum* were completely sequenced and two species (*B. grahamii* and *B. tribocorum*) contain plasmid. The first genomes have been described for *B. henselae* and *B. quintana* with 1.9 and 1.6 Mb, respectively[24], followed by the sequencing of the genomes of *B. bacilliformis* (1.4 Mb) (the Institute for Genomic Research, unpublished), *B. clarridgeiae* (1.5 Mb)[25], *B. grahamii* (2.3 Mb)[26], *B. tribocorum* (2.6 Mb)[27], *B. rattismassiliensis* (2.0 Mb)[28], *B. rattaustraliani* (2.1 Mb)[29], *B. birtlesii* (1.8 Mb)[30] and *B.*

quintina (1.6 Mb)[31] among others. The guanine-cytosine content of *Bartonella* species range from 38.5 mol% for *B. quintana* to 41.1 mol% for *B. vinsonii*[2]. Additionally, some species such as *B. bacilliformis*, *B. henselae*, *B. quintana* and *B. vinsonii* subsp. *berkhoffii* have been shown to contain phage[32]. The phage particles from *B. bacilliformis* and *B. vinsonii* subsp. *berkhoffii* were tailed, whereas those from *B. henselae* and *B. quintana* lacked tails, but all contained 14 kb linear, double-stranded DNA, packaged in a round to head.

To date, *Bartonella* species are identified using standard polymerase chain reaction (PCR) amplification and a sequencing targeting two housekeeping genes (gltA and rpoB) and the internal transcribed spacer fragment[2].

4. Hosts and reservoirs

Bartonella species may show either low specificity with some species infecting several different host species, while some other species show high specificity by infecting a single host. For example, *B. bovis* generally infects only one ruminant species and is seldom associated with other animals. The prevalence of *Bartonella* in both wild and domestic mammals has been studied in many different countries. To date, several animal species have been reported as a potential reservoir hosts, such as cats, dogs, rabbits, ruminants, monkeys, marsupials, marine mammals, bats, insectivores and rodents[19,33].

4.1. Rodents

Wild rodents are known to be important reservoir hosts of various pathogens, which are causative of human illnesses including Bartonellosis. Of the current species of the genus *Bartonella*, fifteen species including *B. birtlesii*, *Bartonella elizabethae (B. elizabethae)*, *B. coopersplainsensis*, *B. doshiae*, *B. grahamii*, *B. japonica*, *B. phoceensis*, *B. queenslandensis*, *B. rattaustraliani*, *B. rattimassiliensis*, *B. silvatica*, *B. taylorii*, *B. tribocorum*, *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *vinsonii*, *B. washoensis* have been isolated from various rodent species[2]. Of these, *B. birtlesii*, *B. elizabethae*, *B. grahamii*, and *B. washoensis* are causative agent of human illnesses.

In Asia, the occurrence of *Bartonella* infection in rodent populations have been reported in several countries including China, Japan, Taiwan, Lao PDR, Cambodia, Thailand, Indonesia, Bangladesh and Israel. *Bartonella* is present in most surveyed rodent populations, with an overall prevalence in the sites investigated ranging from 6% in Korea[34] to 47% in China[35]. Table 2 summarizes *Bartonella* species, host species and geographic distribution of *Bartonella* in Asia. *Bartonella* infections are highly prevalent in rodents in China, Korea, Japan, Russia and Taiwan ranging from 8.6% to 82.3%. Several *Rattus* species have been found as highly infected including the house rat *Rattus tanezumi (R. tanezumi)*. Several species of the

Table 2

Bartonella infection and host species in East Asia.

Country	*Bartonella* infection	Diagnostic test		Host species and prevalence of each species	Type of animal				Reference
		PCR	Culture		Rodent	Shrew	Bat	Exotic pet	
China	*B. elizabethae*	+	+	*Rattus tanezumi* subsp. *flavipectus*, 41.4% (24/58)	+	−	−	−	[35]
	B. grahamii	+	+	*Rattus norvegicus*, 42.9% (3/7)	+	−	−	−	[35]
	B. tribocorum	+	+	*Apodemus chevrieri*, 62.5% (20/32)	+	−	−	−	[35]
				Apodemus draco, 33.3% (2/6)	+	−	−	−	[35]
				Apodemus latronum, 71.4% (5/7)	+	−	−	−	[35]
				Eothenomys miletus, 18.8% (3/16)	+	−	−	−	[35]
	B. grahamii	+	−	*R. rattus*, 28.6% (2/7)	+	−	−	−	[81]
	Bartonella unknown species	+	−	*Rattus losea*, 31% (14/45)	+	−	−	−	[81]
				Rattus norvegicus, 30% (7/23)	+	−	−	−	[81]
				Suncus murinus, 16% (7/43)	+	−	−	−	[81]
				Niviventer confucianus, 4% (1/28)	+	−	−	−	[81]
				Apodemus agrarius, 46.8% (90/192)	+	−	−	−	[81]
				Apodemus peninsulae, 28.6% (2/7)	+	−	−	−	[81]
				Eothenomys melanogaster, 24% (9/37)	+	−	−	−	[81]
				Microtus fortis, 22% (2/9)	+	−	−	−	[81]
Japan	*B. grahamii*	+	+	*Apodemus speciosus*, 51.2% (116/224)	+	−	−	−	[82]
				Apodemus argenteus, 37.1% (13/35)					
	B. phoceensis	+	+	*R. rattus*, 3.7% (11/297)	+	−	−	−	[82]
	B. rattimassiliensis	+	+	*R. rattus*, 1.0% (3/297)	+	−	−	−	[82]
	B. taylorii	+	+	*Apodemus speciosus*, 8.9% (2/224)	+	−	−	−	[82]
				Myodes rufocanus subsp. *bedfordiae*, 23.5% (4/17)					
	B. tribocorum	+	+	*Apodemus speciosus*, 1.8% (4/224)	+	−	−	−	[82]
				Apodemus argenteus, 5.7% (2/35)					
				R. rattus, 2.0% (6/297)					
	Unknown species	+	+	*Apodemus speciosus*, 8.0% (18/224)	+	−	−	−	[82]
				Apodemus argenteus, 11.4% (4/35)					
	B. clarridgeiae	+	+	*Spermophilus dauricus*, 40% (4/10)	−	−	−	+	[48]
	B. elizabethae	+	+	*Sciurus vulgaris* subsp. *orientis*, 20% (2/10)	−	−	−	+	[48]
	B. grahamii	+	+	*Tamias sibiricus*, 41.4% (12/29)	−	−	−	+	[48]

continued Table 2

	B. washoensis	+	+	*Pteromys volans*, 50% (5/10)	−	−	−	+	[48]
				Callosciurus notatus, 63.3% (19/30)	−	−	−	+	[48]
				Tamiasciurus hudosonicus, 16.7% (3/18)	−	−	−	+	[48]
				Glaucomys volans, 60% (6/10)	−	−	−	+	[48]
				Pachyuromys duprasi, 72.2% (13/18)	−	−	−	+	[48]
				Acomys cahirinus, 9.7% (3/31)	−	−	−	+	[48]
				Acomys russatus, 61.5% (8/13)	−	−	−	+	[48]
				Psammomys obesus, 60% (6/10)	−	−	−	+	[48]
				Sekeetamys calurus, 100% (10/10)	−	−	−	+	[48]
				Gerbillus pyramidum, 90% (9/10)	−	−	−	+	[48]
				Jaculus orientalis, 81.3% (13/16)	−	−	−	+	[48]
				Jaculus jaculus,75% (6/8)	−	−	−	+	[48]
Korea	*B. elizabethae*	+	−	*Apodemus agrarius*, 14.2% (53/373)	+	−	−	−	[43]
				Eothenomys melanogaster, 11.1% (1/9)	+	−	−	−	[43]
				Crocidura lasiura, 12.1% (4/33)	−	+	−	−	[43]
	B. elizabethae	+	+	*Apodemus agrarius*, 6.7% (24/358)	+	−	−	−	[34]
Taiwan	*B. elizabethae*	+	−	*R. rattus*, 33.3% (1/3)	+	−	−	−	[73]
	B. tribocorum	+	−	*Rattus norvegicus*, 9.4% (5/53)	+	−	−	−	[73]
	B. elizabethae	+	+	*R. tanezumi* (*R. rattus*), 20% (1/5)	+	−	−	−	[42]
	B. queenslandensis	+	+	*Rattus norvegicus*, 36% (22/61)	+	−	−	−	[42]
	B. phoceensis	+	+	*Sciurus murinus*, 20% (4/20)	−	+	−	−	[42]
	B. rattimassiliensis	+	+						[42]
	B. tribocorum	+	+						[42]
	B. elizabethae	+	+	*R. rattus*, 10% (1/10)	+	−	−	−	[74]
	B. grahamii	+	+	*Rattus norvegicus*, 52.7% (89/169)	+	−	−	−	[74]
	B. phoceensis	+	+	*Rattus losea*, 66.7% (2/3)	+	−	−	−	[74]
	B. rattimassiliensis	+	+	*Sattus murinus*, 28.6% (36/126)	−	−	−	−	[74]
	B. tribocorum	+	+						[74]
	B. elizabethae	+	+	*Miniopterus schreibersii*, 42.9% (6/14)	−	−	+	−	[47]
	B. grahamii	+	+	*Rattus coxinga niviventer*, 100% (1/1)	+	−	−	−	[47]
	B. rattimassiliensis	+	+	*Crocidura attenuata tanakae*, 77.8% (7/9)	−	+	−	−	[47]
	B. tribocorum	+	+						[47]
	unknown species	+	+						[47]
Western	*B. grahamii*	+	−	*Myodes rutilus*, 14.1% (11/78)	+	−	−	−	[85]
Siberia	*B. taylorii*	+	−	*Myodes glareolus*, 16% (4/25)	+	−	−	−	[85]
Russia	*Bartonella* unknown species	+	−						[85]

genera *Apodemus*, *Eothenomys*, *Mus* and *Myodes* have also been shown to host *Bartonella*. A high diversity of *Bartonella* species was observed from rodents in this region including *B. elizabethae*, *B. grahamii*, *B. queenslandensis*, *B. phoceensis*, *B. rattimassiliensis*, *B. taylorii, B. tribocorum* and unknown species.

In Southeast Asia, *Bartonella* species have been investigated from rodents in Indonesia, Lao PDR, Cambodia and Thailand[36–40] (Table 3). Again, the genus *Rattus* appears to be the more prevalent rodent genus followed by the genera *Bandicota* and *Mus*. In South and West Asia, studies of *Bartonella* in rodents are more limited (Table 4).

Altogether, it appears that *B. coopersplainsensis* is mainly found in *Bandicota* species [*Bandicota indica* (*B. indica*) and *Bandicota savilei* (*B. savilei*)] and *R. tanezumi*; *B. elizabethae* in *Apodemus agrarius* and *Rattus* species [*Rattus rattus* (*R. rattus*) and *R. tanezumi*]; *B. grahamii* in *Rattus norvegicus*; *B. queenslandensis* in *Mus* species [*Mus cookii* (*M. cookii*), *B. phoceensis* in *R. tanezumi*, *B. rattimassiliensis* in *M. cookii* and *R. tanezumi*; *B. rochalimae* in *Mus cervicolor*; *B. silvatica* in *Clethrionomys rufocanus*; *B. taylorii* in *C. rufocanus*; *B. tribocorum* in *Apodemus* species (*A. chevrieri*, *A. latronum*) and in *Rattus* species (*R. tanezumi*, *Rattus norvegicus*); *B. washoensis* in *Pachyuromys duprasi*.

4.2. Shrews

Several shrew species live in the domestic areas or peri-domestic environments such as agricultural areas. Isolation of *Bartonella* from shrews has been carried out in Asia and North America. In Asia, most *Bartonella* infections in shrews have been described in East Asia (Korea and Taiwan) and South Asia (Bangladesh and Nepal)[41–43]. In Southeast Asia, the prevalence of *Bartonella* in shrews has been reported in *Sattus murinus* in Indonesia[37] (Table 3). Potential new species of *Bartonella* has been recently observed in *Sattus murinus* in Cambodia[36].

Finally, it appears that *Sattus murinus* is a main host for *B. elizabethae*, *B. phoceensis*, *B. rattimassiliensis* and *B. tribocorum*, although *Crocidura attenuata* is found infected with high prevalence by *B. rattimassiliensis* and *B. tribocorum*.

4.3. Bats

The knowledge of *Bartonella* in bats is still scarce, with only few studies published concerning bats from Asia[44]. Studies on bats and their arthropod vectors have

Table 3

Bartonella infection and host species in Southeast Asia.

Country	*Bartonella* infection	Diagnostic test		Host species and prevalence of each species	Type of animal				Reference
		PCR	Culture		Rodent	Shrew	Bat	Exotic pet	
Cambodia	*B. coopersplainsensis*	+	+	*B. savilei*, 9.5% (7/74)	+	−	−	−	[36]
	B. elizabethae	+	+	*Berylmys berdmorei*, 9.1% (1/11)	+	−	−	−	[36]
	B. queenslandensis	+	+	*Maxomys surifer*, 1.1% (1/92)	+	−	−	−	[36]
	B. rattimassiliensis	+	+	*Niviventer fulvescens*, 10% (1/10)	+	−	−	−	[36]
	B. tribocorum	+	+	*Rattus argentiventer*, 9.5% (4/42)	+	−	−	−	[36]
	Unknown new species	+	+	*Rattus exulans*, 3.5% (4/115)	+	−	−	−	[36]
		+	+	*R. tanzumi phylogenetic R3*, 24.8%(29/117)	+	−	−	−	[36]
		+	+	*Sciurus murinus*, 5.1% (2/39)	−	+	−	−	[36]
Indonesia	*B. phoceensis*	+	−	*R. tanezumi* (*R. rattus*), 10.3% (8/78)	+	−	−	−	[37]
	B. rattimassiliensis	+	−	*Rattus norvegicus*, 2% (1/49)	+	−	−	−	[37]
				S. murinus, 4.8% (4/83)	−	+	−	−	[37]
Laos	*B. elizabethae*	+	−	*R. tanezumi* (*R. rattus*), 16% (61/381)	+	−	−	−	[38]
	B. phoceensis	+	−	*Rattus exulans*, 21.5% (17/79)	+	−	−	−	[38]
	B. tribocorum	+	−	*Cannomys badius*, 50% (1/2)	+	−	−	−	[38]
				Mus cervicolor, 1.4% (1/71)	+	−	−	−	[38]
				Mus caroli, 33.3% (1/3)	+	−	−	−	[38]
	B. coopersplainsensis	+	+	*B. savilei*, 7.1% (1/14)	+	−	−	−	[36]
	B. elizabethae	+	+	*Berylmys berdmorei*, 20% (1/5)	+	−	−	−	[36]
	B. queenslandensis	+	+	*Mus caroli*, 4.8% (1/23)	+	−	−	−	[36]
	B. rattimassiliensis	+	+	*M. cookii*, 30.9% (17/55)	+	−	−	−	[36]
	B. tribocorum	+	+	*Rattus andamanensis*, 40% (2/5)	+	−	−	−	[36]
	Unknown new species	+	+	*R. tanezumi*, 21.8% (17/78)	+	−	−	−	[36]
Thailand	*B. queenslandensis*	+	−	*B. savilei*, 6.1% (2/33)	+	−	−	−	[39]
	B. coopersplainsensis	+	−	*R. tanezumi* (*R. rattus*), 8.2% (4/49)	+	−	−	−	[39]
	B. phoceensis	+	−	*Rattus exulans*, 1.5% (1/69)	+	−	−	−	[39]
	B. rochalimae	+	−	*Mus cervicolor*, 50% (1/2)	+	−	−	−	[39]
	Candidatus Bartonella	+	+	*Berylmys berdmorei*, 25% (5/20)	+	−	−	−	[39]
	thailandensis	+	+	*Maxomys surifer*, 24.3% (8/33)	+	−	−	−	[39]
	B. elizabethae	+	+	*B. indica*, 8.1% (12/147)	+	−	−	−	[40]
	B. grahamii	+	+	*R. tanezumi* (*R. rattus*), 12.5% (3/24)	+	−	−	−	[40]
				Rattus losea, 18% (2/11)	+	−	−	−	[40]
	B. coopersplainsensis	+	+	*B. indica*, 32.6% (15/46)	+	−	−	−	[86]
	B. elizabethae	+	+	*B. savilei*, 57.1% (4/7)	+	−	−	−	[86]
	B. phoceensis	+	+	*R. tanezumi* (*R. rattus*), 65.2% (88/135)	+	−	−	−	[86]
	B. rattimassiliensis	+	+	*Rattus exulans*, 3.2% (3/95)	+	−	−	−	[86]
	B. tribocorum	+	+	*Rattus losea*, 33.3% (1/3)	+	−	−	−	[86]
		+	+	*R. norvegicus*, 86.4% (19/22)	+	−	−	−	[86]
		+	+	*Rattus argentiventer*, 66.7% (2/3)	+	−	−	−	[86]
		+	+	*Rattus remotus*, 50% (1/2)	+	−	−	−	[86]
		+	+	*Mus cervicolor*, 42.9% (3/7)	+	−	−	−	[86]
		+	+	*Berylmys berdmorei*, 100% (1/1)	+	−	−	−	[86]
	B. coopersplainsensis	+	+	*B. indica*, 7.7% (5/65)	+	−	−	−	[36]
	B. elizabethae	+	+	*Berylmys berdmorei*, 13.3% (2/15)	+	−	−	−	[36]
	B. phoceensis	+	+	*Mus caroli*, 8% (2/26)	+	−	−	−	[36]
	B. queenslandensis	+	+	*M. cookii*, 17.1% (6/35)	+	−	−	−	[36]
	B. rattimassiliensis	+	+	*Mus cervicolor*, 20.8% (10/48)	+	−	−	−	[36]
	B. tribocorum	+	+	*Mus* sp., 75% (3/4)	+	−	−	−	[36]
		+	+	*Niviventer fulvescens*, 12.5% (1/8)	+	−	−	−	[36]
		+	+	*Rattus exulans*, 4.2% (6/142)	+	−	−	−	[36]
		+	+	*R. tanezumi*, 31.6% (12/38)	+	−	−	−	[36]
		+	+	*R. tanezumi R3*, 20.7% (6/29)	+	−	−	−	[36]

demonstrated that bats were infected with unknown *Bartonella* species[45]. Another study found new putative species in bats from Kenya[46]. In Asia, reports are even scarcer. *Bartonella* infection in bat has been described in Taiwan[47]. Six blood samples of *Miniopterus schreibersii* were positive with new putative *Bartonella* spp. with high prevalence (42.9%, Table 2).

4.4. Exotic pets

Exotic pets are wildlife that are traded around the world, with important illegal trafficking, and have been (and still being) imported into many countries. The illegal trade without quarantine may cause the dissemination of infectious diseases. However, there are little data on

Table 4

Bartonella infection and host species in South and West Asia.

Country	*Bartonella* infection	Diagnostic test		Host species	Type of animal				Reference
		PCR	Culture		Rodent	Shrew	Bat	Exotic pet	
Bangladesh	*B. elizabethae*	+	+	*Bandicota bengalensis*, 63.2% (48/76)	+	−	−	−	[37]
	B. tribocorum	+	+	*R. rattus*, 32.3% (32/99)	+	−	−	−	[37]
				Sciurus murinus, 42.9% (6/14)	−	+	−	−	[37]
Nepal	*B. elizabethae*	+	−	*B. bengalensis*, 26.3% (10/38)	+	−	−	−	[87]
	B. queenslandensis	+	−	*R. rattus brunneusculus*, 43.3% (39/90)	+	−	−	−	[87]
	B. phoceensis	+	−	*Sciurus murinus*, 64.1% (59/92)	−	+	−	−	[87]
	B. rochalimae	+	−						[87]
	B. rattimassiliensis	+	−						[87]
	B. tribocorum	+	−						[87]
Israel	*B. elizabethae*	+	+	*R. rattus*, 16% (10/62)	+	−	−	−	[88]
	B. tribocorum	+	+						[88]
	B. elizabethae	+	−	*Apodemus cahirinus*, 25% (1/4)	+	−	−	−	[89]
	B. tribocorum	+	−	*R. rattus*, 24% (19/79)	+	−	−	−	[89]

Table 5

Species of *Bartonella* detected on arthropod vectors from rodents and shrews in Asia.

Country	*Bartonella* infection	Diagnostic test	Vector species	Type of vector	Host reservoirs	Ref
Afghanistan	*B. elizabethae*	PCR	*Xenopsylla cheopis*	flea	*Cricetulus migratorius*	[90]
	B. dosiae	PCR	*Xenopsylla cheopis*	flea	*Meriones lybicus* (gerbil)	[90]
	B. koehlerae	PCR	*Xenopsylla cheopis*	flea	*Mus* spp.	[90]
	B. quintana	PCR	*Xenopsylla cheopis*	flea	*Rattus* spp.	[90]
	B. taylorii	PCR	*Xenopsylla cheopis*	flea		[90]
China	*B. tribocorum*	PCR	*Xenopsylla cheopis*	flea	*Rattus tanezumi* subsp. *flavipectus*	[91]
		PCR	*Ctenophthalmus lushuiensis*	flea	*Eothenomys* spp.	[91]
Korea	*Bartonella* spp.	PCR	*Haemaphysalis longicornis*	tick	Wild rodents	[34]
		PCR	*Haemaphysalis flava*	tick	Unidentified species	[34]
		PCR	*Ixodes nipponensis*	tick		[34]
		PCR	*Ixodes turdus*	tick		[34]
		PCR	*Ixodes persulcatus*	tick		[34]
		PCR	*Ixodes* spp.	tick		[34]
		PCR	*Ctenophthalmus congeneroides*	flea	*Apodemus agrarius*, *Crocidura lasiura*, *Microtus fortis*, *Myodes regulus*, *Micromys minutus*, *Mus musculus*	[92]
		PCR	*Stenoponia sidimi*	flea		[92]
Israel	*Bartonella* sp.	PCR	*Xenopsylla cheopis*	flea	*R. rattus*	[93]
		PCR	*Leptopsylla algira*	flea	*Mus musculus*	[93]
		PCR	*Xenopsylla ramesis*	flea	*Meriones tristrami*	[93]
		PCR	*Synosternus cleopatrae*	flea	*Gerbillus andersoni allenbyi*	[93]
		PCR			*Gerbillus pyramidum*	[93]
		PCR			*Meriones sacramenti*	[93]
Taiwan	*Bartonella* spp.	PCR	*Laelaps* spp.	mite	*Apodemus cahirinus*	[42]
		PCR	*Laelaps echianinus*	mite	*Rattus norvegicus*	[42]
		PCR	*Xenopsylla cheopis*	flea	*R. rattus*	[42]
		PCR	*Polyplax spinulosa*	lice	*Sciurus murinus*	[42]
		PCR	*Dermacentor* spp.	tick		[42]
		PCR	*Ixodes* spp.	tick		[42]
Thailand	*Bartonella* BNfRs	PCR	*Nosopsyllus fasciatus*	flea	*Rattus surifer*	[94]
	B. tamiae	PCR	*Leptotrombidium* spp.	mite	*Rattus argentiventer*	[49]
		PCR	*Schoengastia* spp.	mite	*R. rattus*	[49]
		PCR	*Blankarrtia* spp.	mite	*B. indica*	[49]
		PCR	*Haemaphysalis* spp.	tick	*B. savilei*	[49]
		PCR			*Mus cervicolor*	[49]

prevalence of infection with *Bartonella* spp. from exotic small mammal pets in Asia (Table 2). Among them, a study reported that several exotic species in Japan were infected with *Bartonella* spp. with quite high prevalence[48].

4.5. Vectors

Several blood-sucking arthropods including fleas, mites, sandflies and ticks have been reported as potential vectors transmitting *Bartonella* among animals and between animals and humans.

Of the several blood-sucking arthropods, fleas are the key vectors of *Bartonella* infection. Several studies have suggested that fleas, especially *Xenopsylla cheopis*, are potential vectors in rodents (Table 5). Ticks, mites and lice are also potential vectors for *Bartonella* infections in

Table 6

Case reports of *Bartonella* infection in Asia.

Country	*Bartonella* infection	Diagnostic test	Clinical sign	Patient	Ref
India	*B. quintana*	Culture, serology	endocarditis	endocarditis patients	[95]
Japan	*B. henselae*	Culture, PCR	endocarditis	77- year-old, male	[96]
	B. quintana	Serology	fever, headache, anorexia, history of body lice and fleas infestation	homeless people, male and female	[97]
	B. quintana	Culture, PCR	endocarditis	70- year-old, female	[98]
	B. quintana	Culture, PCR	endocarditis	66-year-old, male	[99]
Jordan	*B. quintana*	Serology, PCR	None (Seroprevalence among Jordanian children)	None	[100]
	B. henselae	Serology, PCR		None	[100]
Korea	*B. henselae*	Gram staining, PCR	fever, enlargement of axillary lymph nodes	8-year-old, girl	[101]
	B. henselae	Serology	cervical lymphadenitis	25- year-old, female	[101]
Nepal	*B. elizabethae*	Serology	headache, fever, myalgia	ranging from 9 to 70 years, both male and female	[53]
	B. quintana	Serology	headache, fever, myalgia		[53]
	B. tamiae	Serology	headache, fever, myalgia		[53]
	B. vinsonii arupensis	Serology	headache, fever, myalgia		[53]
Thailand	*B. elizabethae*	Serology	febrile patients, fever > 38 ℃ for < 2 weeks	febrile patients, ≥7 years old	[52]
	B. henselae	Serology	non-febrile patients, (unidentified)	non-febrile patients, ≥14 years old	[52]
	B. quintana	Serology			[52]
	B. henselae	Culture, PCR	fever, pharyngitis, meningitis	febrile patients	[50]
	B. henselae	Culture, PCR	having symptomatic HIV infection	40 year-old	[102]
	B. tamiae	Culture, PCR	fatigue, myalgia, fever, headache	38 year-old	[8]
	B. tamiae	Culture, PCR	pterygium in each eye	41 year-old	[8]
	B. tamiae	Culture, PCR	fever, fatigue, myalgia, a headache	12 year-old	[8]
	B. vinsonii	Culture, PCR	headache, myalgias, dizziness, and fatigue	11 to 56 year-old	[59]

rodents. Epidemiological surveys of *Bartonella* infection in ticks, mites and lice have been done in Korea, Taiwan and Thailand[16,34,42,49].

6. Zoonotic diseases and case reports in Asia

Bartonella species are important zoonotic bacteria with increasing array of emerging infections in humans and animals. Bartonellosis has been described in Asia. Possible routes of transmission are contacts with infected animals or blood-sucking arthropod via their feces. Four *Bartonella* species including *B. henselae*, *B. quintana*, *B. elizabethae* and *B. tamiae* have been reported as causative agents of several human diseases in Asia (Table 6). However, few cases of human infections with *Bartonella* bacteria of rodent origins have been reported. The first case of *Bartonella* endocarditis in Thailand was found in a 57-year-old male poultry farmer in Khon Kaen province, where the source of pathogen was a cat. *B. tamiae* was isolated from three febrile patients in Thailand[8]. In another report, several farmers were supposed to be exposed to infected rodents at home or fields[50]. Recently, four patients were found infected by *B. vinsonii* in Northern and Northeastern Thailand, with dogs and rats supposed to be reservoirs[51]. Additional serological studies evidenced exposure to rodent *Bartonella* spp. in Thailand but also in Nepal[52,53]. However, to date, only *B. elizabethae* was found in rodent surveys, where the most common rodents were murid from *Apodemus* spp. and *Rattus* spp. (and particularly the commensal *R. rattus* and *R. tanezumi*).

7. Perspectives

The diversity of *Bartonella* species is far from being known as the recent study of Jiyipong *et al*. emphasized on three new putative species[36]. Indeed, Southeast Asia is a hotspot of mammal species[54] and a diversification centre for several rodent families. Two-thirds of living rodent species belongs to the family Muridae[55], which also represents most of the rodents found in Southeast Asia with 35 species[56]. It appears that less than 50% of these murid species have been investigated for the presence of *Bartonella* species (Table 3). The knowledge is even poorer for shrews and bats. This emphasizes the need to increase the screening, detection and characterization of *Bartonella* in small mammals[57].

Since *Bartonella* species may be transmitted to humans by ticks, fleas and lice, surveys of *Bartonella* distribution within arthropods are needed. In particular, the population changes of these vectors of *Bartonella* in relation to the impacts of habitat and land-use changes should be better investigated[57].

Rodents, shrews and bats live in a wide range of habitats that are frequented by humans[58], which warrants further investigations on the transmission ecology of *Bartonella* in order to improve prevention of *Bartonella* infections. Identification of risky habitats for human transmission is needed to develop a surveillance strategy, which could be done only after the improvement of our knowledge on the diversity of *Bartonella* in small mammals and in their arthropod vectors.

This review by giving up-to-date list of reservoirs will help develop a strategy of reservoirs, vectors and habitats

prone to be sources of outbreaks and/or emerging *Bartonella* infections in humans.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

Bartonella is an important bacteria that can make various infections in different animals specially humans. This bacteria has various hosts and it is transmitted by several vectors. Species of *Bartonella* are Gram-negative intracellular bacteria that infects erythrocytes of various mammalian and non-mammalian animals and mainly transmitted by blood-sucking arthropod vectors.

Research frontiers

This is a review article about *Bartonella* infection in small mammals including rodents, insectivores, bats and exotic small mammal pets and their vectors in Asia. This article dicusses the present species of *Bartonella* in animals cited.

Related reports

This is a review article and it is based on various reports that are already reported. Various articles mentioned role of different species of *Bartonella* in making infections in animals (mammals and non-mammals). *Bartonella* in different animals have been recognized.

Innovations and breakthroughs

This review article investigates various species of *Bartonella* in animals that already a little have been studied and can offer good information about the role of *Bartonella* at causing infection in animals cited.

Applications

This review article surveys prevalence of various species of *Bartonella* in different areas of Asia. Informations offered in this article can be useful for more studies in future.

Peer review

This is a good research about the presence of various species of *Bartonella* and its role at causing different infections. The consideration of authors to various reservoirs of this bacteria in animals that a little have been already surveyed is interesting. Diagnostic tests referred in this article are very useful.

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